UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/064,512	07/23/2002	Loree Heller	1372.48	6625

21901 7590 05/11/2005

SMITH & HOPEN PA
15950 BAY VISTA DRIVE
SUITE 220
CLEARWATER, FL 33760

EXAMINER	
WHITEMAN, BRIAN A	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 05/11/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/064,512	HELLER ET AL.	
	Examiner	Art Unit	
	Brian Whiteman	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 October 2004 and 25 February 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11* is/are pending in the application.

4a) Of the above claim(s) *3-5* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,6-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/28/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

RD

DETAILED ACTION

Final Rejection

Claims 1-11 are pending.

Applicant's traversal, the amendment to claims 1, 2, and 6-10 and the amendment to the specification in paper filed on 10/28/04 and the correct listing of claims filed on 2/25/05 is acknowledged and considered.

Election/Restrictions

Claims 3, 4, and 5 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 6/7/04.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2, and 6-11 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating a tumor *in vivo* comprising identifying an individual with a tumor; intratumorally introducing at least one non-coding nucleic acid sequence; to at least one tumor the individual and applying an energy source to the at least one tumor transfected with the non-coding nucleic acid sequence, does not reasonably provide enablement for a method of treating a tumor in vivo comprising introducing at least one

non-coding nucleic acid to at least one tumor using a genus of administration routes and applying an energy source to the at least one tumor. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

> Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in In re Wands, 858 F.2d 731, 8USPQ2d 1400 (Fed. Cir. 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The claimed invention reads on a method of treating a tumor *in vivo* comprising identifying an individual with a tumor; introducing at least one non-coding nucleic acid to either the extracellular or intracellular space of a tumor in the individual; and applying an energy source to the tumor. The claimed invention lies in the field of cancer gene therapy.

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the application coupled with information known in the art without undue experimentation (United States v. Technologies Inc., 8 USPQ2d 1217 (Fed. Cir. 1988). Whether undue experimentation is required is not based upon a single factor, but rather a conclusion reached by many factors. These factors were outlined in Ex parte Forman, 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and again in In Re Wands (see above) and include the following:

Furthermore, and with respect to claims directed to any nucleic acid useful for gene therapy and directed to any treatment of an individual; the state of the art for gene therapy, exemplified by Anderson et al., *Nature*, Vol. 392, pp. 25-30, 1998, displays major consideration for any gene transfer or any DNA therapy protocol involve issues that include:

1) The type of vector and amount of DNA constructs to be administered,

2) The route and time course of administration, the sites of administration, and successful uptake of the claimed DNA at the target site;

3) The trafficking of the genetic material within cellular organelles, the rate of degradation of the DNA, the level of mRNA produced, the stability of the mRNA product, the amount and stability of the protein produced, and

4) What amount of the expressed proteins considered to be therapeutically effective for a DNA therapy method.

In addition, all of these issues differ dramatically based on the specific vector used, the route of administration, the animal being treated, therapeutically effective amount of the DNA, and the disease being treated.

Anderson teaches that gene therapy is a powerful new technology that still requires several years before it will make a noticeable impact on the treatment of disease, and that several major deficiencies still exist including poor delivery systems, both viral and non-viral, and poor gene expression after genes are delivered (pp. 25-30).

Anderson further teaches that the reason for the low efficiency of gene transfer and expression in human patients is that we still lack the basis understanding of how vectors should be constructed what regulatory sequences are appropriated for which cell types (page 30, column 1, last paragraph). Furthermore, Verma, *Nature*, Vol. 389, pages 239-242, 1997, indicates that factors including the nature of the diseases and/or disorders, the nature of a DNA and/or target tissue, and a delivery system and/or amounts of the DNA complexes employed in the delivery system that would generate a therapeutic effect *in vivo* must be considered for any gene therapy method to be successful (page 238, columns 1 and 2).

In further view of the doubts expressed above by Anderson and Verma, the state of the art for cancer gene therapy as discussed by Vile et al., (Gene Therapy, Vol. 7, pp. 2-8, 2000). Vile teaches:

> The problems which gene therapy for cancer will take into the next millennium focus far less on the choice of therapeutic gene(s) to be used than on the means of delivering them. There is already a battery of genes that we know are very effective in killing cells, if they can be expressed at the right site and at appropriate levels. Nonetheless, until the perfect vector is developed, the choice of gene will remain crucially important in order to compensate for the deficiencies of the vectors we currently have available (page 2, 1st paragraph, left column). Whatever its mechanism, no single genes can be a serious contender unless it has a demonstrable bystander effect (page 2, right column). The requirement for such a bystander effect stems directly from the poor delivery efficiency provided by current vectors (page 2, right column).
>
> A genuine ability to target delivery systems to tumor cells distributed widely throughout the body of a patient would simultaneously increase real titers and efficacy. In truth, no such systemically targeted vectors exist yet. Injection of vectors into the bloodstream for the treatment of cancer requires not only that the vectors be targeted (to infect only tumor cells) but also that they by protected (from degradation, sequestration or immune attack) for long periods of time so that they can reach the appropriate sites for infection. Moreover, having reached such sites, the vectors must be able to penetrate into the tumor from the bloodstream before carrying out their targeted infection (page 4, bottom left column and top right column).

Thus, at the time the application was filed, the state of the art for gene therapy was considered highly unpredictable.

The claimed method reads on using any route for introducing at least one nucleic acid to at least one tumor. More specifically, claims, 1, 2, and 4-10 read on delivering a non-coding nucleic acid to at least one tumor in the subject. In addition, claim 11 further comprises delivering a nucleic acid encoding a therapeutic protein to the tumor. The unpredictability of the art is supported by the art of record; see Anderson, Verma, and Vile. The unpredictability involves poor and inefficient delivery of nucleic acid to target cells in vivo, host immune responses which limit the ability of the nucleic acid to infect target cells, uptake into other tissues

instead of uptake into target tumor cells. The prior art teaches that the drug (e.g., nucleic acid) and electric pulses must be present and the specification as filed does not teach one skilled in the art how to deliver the nucleic acid to at least one tumor using a genus of administration routes so that the nucleic acid and electric pulse are present. See Heller et al. Advanced Drug Delivery 35: 119-129, 1999. The applicants teach injecting an empty plasmid directly into a tumor of a group of mice and applying an electrical pulse to the tumor (not the nucleic acid). The results obtained indicated that the group of mice treated with an empty plasmid followed by electrical treatment had reduced tumor volumes relative to other treatment groups. However, the relevance of this data to treatment of at least one tumor in an individual by delivering at least one nucleic acid using a genus of administration routes is unclear at best because neither the applicants nor the prior art provide a correlation or nexus between delivering a nucleic acid directly to a tumor in vivo such as the in the working example provided by applicants with results which the skilled artisan would reasonably expect to see in vivo using a genus of administrations. The teachings in the specification do not commensurate with the scope of the claims. The invention involves one of the most complex areas of medicine/molecular biology, gene therapy for the treatment of a tumor in an individual. Given the above analysis of the factors which the courts have determined are critical in determining whether a claimed invention is enabled, it is concluded that the skilled artisan would only have been enabled to use direct delivery of the nucleic acid to a tumor in vivo and would have need to have to conduct undue and excessive experimentation in order to practice the full scope of the claimed method using a genus of administration routes.

In conclusion, the as-filed specification and claims coupled with the art of record at the time the invention was made only provide sufficient guidance and/or evidence to reasonably

enable a method of treating a tumor *in vivo* comprising identifying an individual with a tumor; introducing by intra-tumoral injection at least one non-coding nucleic acid; and applying an energy source to the tumor transfected with the non-coding nucleic acid and does not provide sufficient guidance and/or factual evidence for one skilled in the art to practice the full scope of the claimed invention. Given that gene therapy wherein any carrier is employed to correct a disease or a medical condition in an individual was unpredictable at the time the invention was made, and given the lack of sufficient guidance as to a gene therapy effect produced by any nucleic acid cited in the claims, one skilled in the art would have to engage in a large quantity of experimentation in order to practice the claimed invention based on the applicants' disclosure and the unpredictability of gene therapy.

Applicant's arguments filed 10/28/02 have been fully considered but they are not persuasive.

Applicant's argument with respect to the claimed invention does not lie in the field of cancer gene therapy is not found persuasive because the claims (claim 1 and claim 11) are specifically recite delivering a nucleic acid (non-coding nucleic acid and a nucleic acid encoding a therapeutic protein) to at least one tumor. The problems with gene therapy also apply to the claimed invention because the prior art teaches that the drug (e.g., nucleic acid) and electric pulses must be present for the claimed method to be enabled (Heller, supra). The prior art teaches the problems of targeting a specific cell and the applicants only teach direct administration to a tumor cell. As stated above, the relevance of this data to treatment of at least one tumor in an individual by delivering at least one nucleic acid using a genus of administration routes is unclear at best because neither the applicants nor the prior art provide a correlation or

nexus between delivering a nucleic acid directly to a tumor in vivo such as the in the working example provided by applicants with results which the skilled artisan would reasonably expect to see in vivo using a genus of administrations.

Applicant's argument with respect to that the gene delivered to a tumor cell in accordance with the present invention is a non-native gene is not found persuasive because the non-native gene (non-coding nucleic acid) is a nucleic acid sequence and the art of record teaches the unpredictability of delivering any nucleic acid to a targeted cell using a genus of administration routes.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.
> (f) he did not himself invent the subject matter sought to be patented.

Instant Claims read on a method of treating a tumor in a subject comprising administering at least one non-coding nucleic acid to at least one tumor and using electrical pulse on the tumor.

Claims 1, 2, and 6-8 are rejected under 35 U.S.C. 102(b) as being anticipated by Dev et al. (US 5,993,434). Dev teaches delivering nucleic acids to tumor cells and using electrical

pulses on the tumor cells (columns 2, 9, and 11-14). Dev teaches using antisense nucleic acid or triplex agents that are associated with the expression of a gene, nucleic acid sequences that interfere with the gene's expression at the translational level for treating a cell proliferative disorder (columns 8-9). In addition, the step of identifying a subject with a tumor in instant claim 1 would be required for using the method taught by Dev because the subject would have to have a tumor in order for the method to be enabled. Dev teaches the limitation in instant claim 6 (column 6). Dev teaches the limitation in instant claim 7 (column 7). Dev teaches the limitation in instant claim 8 (column 7).

Applicant's arguments with respect to claims 1 and 2 have been considered but are moot in view of the new ground(s) of rejection.

Claims 1, 2, and 6-8 are rejected under 35 U.S.C. 102(e) as being anticipated Dev et al., (US 6,569,149).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Dev teaches delivering nucleic acids to tumor cells and using electrical pulses on the tumor cells (columns 2, 9, and 11-15). Dev teaches using antisense nucleic acid or triplex agents that are associated with the expression of a gene, nucleic acid sequences that interfere with the

gene's expression at the translational level for treating a cell proliferative disorder (columns 8-9). In addition, the step of identifying a subject with a tumor in instant claim 1 would be required for using the method taught by Dev because the subject would have to have a tumor in order for the method to be enabled. Dev teaches the limitation in instant claim 6 (column 6). Dev teaches the limitation in instant claim 7 (column 7). Dev teaches the limitation in instant claim 8 (column 7).

Applicant's arguments filed 10/28/04 have been fully considered but they are not persuasive. Applicant argues that Dev does not describe the use of a non-coding nucleic acid for eliciting an anti-tumor response as described and claimed by the present invention.

Applicant's argument is not found persuasive because Dev teaches using antisense molecule in the method (column 9). Antisense molecules are non-coding nucleic acid sequences that do not encode a therapeutic protein.

Claims 1, 2, and 6-8 are rejected under 35 U.S.C. 102(f) because the applicant did not invent the claimed subject matter. Dev et al., in US Patent 6,569,149 claim a method of introducing molecules into cells of a tissue of a patient having a cell proliferative disorder and applying electric pulses on the tissue to produce an electric field in the tissue, wherein the molecules are nucleic acids (columns 14-15). The claims from '149 do not specifically recite using a non-coding nucleic acid in the method, however, when reading the definition of a nucleic acid in the specification of '149, the nucleic acid embraces antisense nucleic acids (columns 8-9).

Applicant's arguments filed 10/28/04 have been fully considered but they are not persuasive. Applicant argues that Dev does not describe the use of a non-coding nucleic acid for eliciting an anti-tumor response as described and claimed by the present invention.

Applicant's argument is not found persuasive because Dev teaches using antisense molecule in the method (column 9). Antisense molecules are non-coding nucleic acid sequences that do not encode a therapeutic protein.

Claims 1, 2, and 6-8 are rejected under 35 U.S.C. 102(f) because the applicant did not invent the claimed subject matter. Dev et al., in US Patent 5,993,434 claim a method of introducing molecules into cells of a tissue of a patient and applying electric pulses on the tissue to produce an electric field in the tissue, wherein the molecules are nucleic acids (columns 6-9 and 14-15). The claims from '149 do not specifically recite treating a tumor in the patient using a non-coding nucleic acid in the method, however, when the claims in light of the specification, the claims read on treating a tumor a patient (column 2). In addition, when reading the definition of a nucleic acid in the specification of '434, the nucleic acid embraces antisense nucleic acids (columns 8-9).

Applicant's arguments with respect to claims 1 and 2 have been considered but are moot in view of the new ground(s) of rejection.

Claims 1, 2, and 6-8 are rejected under 35 U.S.C. 102(f) because the applicant did not invent the claimed subject matter. Dev et al., in US Patent 6,451,002 claim a method of introducing molecules into cells of a tissue of a patient and applying electric pulses on the tissue

to produce an electric field in the tissue, wherein the molecules are nucleic acids (columns 14-16). The claims from '149 do not specifically recite treating a tumor in the patient using a non-coding nucleic acid in the method, however, when the claims in light of the specification, the claims read on treating a tumor a patient (column 2). In addition, when reading the definition of a nucleic acid in the specification of '002, the nucleic acid embraces antisense nucleic acids (columns 8-9).

Applicant's arguments with respect to claims 1 and 2 have been considered but are moot in view of the new ground(s) of rejection.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various

claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 9, and 10 are rejected under 35 U.S.C. 103(a) as being obvious over Dev et al., (US 5,993,434) taken with Heller et al. (6,714,816).

Dev teaches delivering nucleic acids to tumor cells and using electrical pulses on the tumor cells (columns 2, 9, and 11-14). Dev teaches using antisense nucleic acid or triplex agents that are associated with the expression of a gene, nucleic acid sequences that interfere with the gene's expression at the translational level for treating a cell proliferative disorder (columns 8-9). In addition, the step of identifying a subject with a tumor in instant claim 1 would be required for using the method taught by Dev because the subject would have to have a tumor in order for the method to be enabled. However, Dev does not specifically teach jet injecting the nucleic acid into extracellular space coincident to the tumor.

However, at the time the invention was made, Heller teaches methods for introducing the molecules into the extracellular spaces of tissues such as jet injection and particle bombardment can be used to provide a source of molecules in the extracellular space for delivery using electrical fields (columns 3 and 5).

In addition, it would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Dev taken with Heller, namely to use jet injection into the extracellular space coincident to the tumor. One of ordinary skill in the

art would have been motivated to use jet injection into the extracellular space coincident to the tumor because Heller teaches that can be used to delivery molecules to the extracellular space of a cell (column 3).

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Applicant's arguments with respect to claims 1 and 9-10 have been considered but are moot in view of the new ground(s) of rejection.

Claims 1 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dev et al., (US 5,993,434) taken with Chiocca et al. (US 5,688,773).

Dev teaches delivering nucleic acids to tumor cells and using electrical pulses on the tumor cells (columns 2, 9, and 11-14). Dev teaches using antisense nucleic acid or triplex agents that are associated with the expression of a gene, nucleic acid sequences that interfere with the gene's expression at the translational level for treating a cell proliferative disorder (columns 8-9). In addition, the step of identifying a subject with a tumor in instant claim 1 would be required for using the method taught by Dev because the subject would have to have a tumor in order for the method to be enabled. However, Dev does not specifically teach using a nucleic acid encoding a therapeutic protein and a non-coding nucleic acid sequence that does not encode a therapeutic protein in the same method.

However, at the time the invention was made, Chiocca teaches that the combination of cancer gene therapy methods that have different mode of actions can improve the effectiveness

of cancer gene therapy, including antisense cancer therapy and prodrug gene therapy (column 51).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Dev taken with Chiocca, namely to combine different types of cancer gene therapy methods including combining an antisense cancer therapy and a prodrug gene therapy. One of ordinary skill in the art would have been motivated to combine the therapies to improve the effectiveness of cancer gene therapy because antisense therapy and prodrug gene therapy have different mode of actions. In addition, one of ordinary skill in the art would have been motivated to introduce both the antisense molecule and the prodrug gene at the same time to save time from administering the antisense molecule and prodrug gene at different time points.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Applicant's arguments with respect to claims 1 and 11 have been considered but are moot in view of the new ground(s) of rejection.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground

provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 2, and 6-8 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 2, and 3 of U.S. Patent No. 6,569,149.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims from the instant application are directed to method of treating a tumor in a subject comprising administering at least one non-coding nucleic acid to at least one tumor and using electrical pulses on the tumor and the claims from '149 recite a method of applying an electric field to a tissue of a patient having a malignant cell proliferation disorder for the purpose of introducing a molecule into cells of the tissue to treat the disorder, wherein the molecule is a nucleic acid. The claims from '149 do not specifically recite using a non-coding nucleic acid in the method, however, when reading the definition of a nucleic acid in the specification of '149, the nucleic acid embraces antisense nucleic acids (column 9).

Applicant's arguments filed 10/28/04 have been fully considered but they are not persuasive. Applicant argues that Dev does not describe the use of a non-coding nucleic acid for eliciting an anti-tumor response as described and claimed by the present invention.

Applicant's argument is not found persuasive because Dev teaches using antisense molecule in the method (column 9). Antisense molecules are non-coding nucleic acid sequences that do not encode a therapeutic protein.

Claims 1, 2, and 6-8 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-13 of U.S. Patent No. 6,451,002. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims from the instant application are directed to method of treating a tumor in a subject comprising administering at least one non-coding nucleic acid to at least one tumor and using electrical pulses on the tumor and the claims from '002 recite a method of applying an electric field to a tissue of a patient for the purpose of introducing a molecule into cells of the tissue, wherein the molecule is a nucleic acid. The claims from '002 do not specifically recite using a non-coding nucleic acid in the method, however, when reading the definition of a nucleic acid in the specification of '002, the nucleic acid embraces antisense nucleic acids (column 9). In addition, the claims from '002 do not specifically recite treating a tumor in the patient, however, when reading the specification in light of the claims the claims from '002 read on the instant claims. See column 2 of '002.

Applicant's arguments with respect to claims 1 and 2 have been considered but are moot in view of the new ground(s) of rejection.

Claims 1, 2, and 6-8 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-12 of U.S. Patent No. 5,993,434. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims from the instant application are directed to method of treating a tumor in a subject comprising administering at least one non-coding nucleic acid to at least one tumor and using electrical pulses on the tumor and the claims from '434 recite a method of applying an electric

field to a tissue of a patient for the purpose of introducing a molecule into cells of the tissue, wherein the molecule is a nucleic acid. The claims from '434 do not specifically recite using a non-coding nucleic acid in the method, however, when reading the definition of a nucleic acid in the specification of '434, the nucleic acid embraces antisense nucleic acids (column 9). In addition, the claims from '434 do not specifically recite treating a tumor in the patient, however, when reading the specification in light of the claims the claims from '434 read on the instant claims. See column 2 of '434.

Applicant's arguments with respect to claims 1 and 2 have been considered but are moot in view of the new ground(s) of rejection.

Claims 1, 2, 9 and 10 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 2, and 3 of U.S. Patent No. 6,569,149 in view of Heller et al. (US 6,714,816).

Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims from the instant application are directed to method of treating a tumor in a subject comprising administering at least one non-coding nucleic acid to at least one tumor and using electroporation on the tumor and the claims from '149 recite a method of applying an electric field to a tissue of a patient having a malignant cell proliferation disorder for the purpose of introducing a molecule into cells of the tissue to treat the disorder, wherein the molecule is a nucleic acid. The claims from '149 do not specifically recite using a non-coding nucleic acid in the method, however, when reading the definition of a nucleic acid in the specification of '149, the nucleic acid embraces antisense nucleic acids (column 9).

However, the claims from '149 do not specifically teach jet injecting the nucleic acid into extracellular space coincident to the tumor.

However, at the time the invention was made, Heller teaches methods for introducing the molecules into the extracellular spaces of tissues such as jet injection and particle bombardment can be used to provide a source of molecules in the extracellular space for delivery using electrical fields (columns 3 and 5).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Dev taken with Heller, namely to use jet injection into the extracellular space coincident to the tumor. One of ordinary skill in the art would have been motivated to use jet injection into the extracellular space coincident to the tumor because Heller teaches that can be used to delivery molecules to the extracellular space of a cell (column 3).

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Applicant's arguments with respect to claims 1 and 2 have been considered but are moot in view of the new ground(s) of rejection.

Claims 1, 2, and 6-8 are directed to an invention not patentably distinct from claims 1, 2, and 3 of commonly assigned US patent 6,569,149. Specifically, the claims from the instant specification are directed to delivering non-coding nucleic acids into a tumor cell in vivo using electroporation and the claims from '149 are directed to a method of introducing molecules into

cells of a tissue of a patient having a cell proliferative disorder using electroporation on the tissue, wherein the molecules are anti-sense nucleic acids.

Claims 1, 2, and 6-8 directed to an invention not patentably distinct from claims 1-12 of commonly assigned US Patent 5,993,434. Specifically, for the reasons set forth under the double patenting rejection over claims 1-12 of '434.

Claims 1, 2, and 6-8 directed to an invention not patentably distinct from claims 1-13 of commonly assigned US Patent 6,451,002. Specifically, for the reasons set forth under the double patenting rejection over claims 1-13 of '002.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP § 2302). Commonly assigned patent, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee is required under 35 U.S.C. 103(c) and 37 CFR 1.78(c) to either show that the conflicting inventions were commonly owned at the time the invention in this application was made or to name the prior inventor of the conflicting subject matter. Failure to comply with this requirement will result in a holding of abandonment of the application.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications filed on or after November 29, 1999.

Response to Arguments

Applicant's arguments, see page 7, filed 10/28/04, with respect to 102(e) as being anticipated by Maclaughlin et al. (US 2002/0102729) have been fully considered and are persuasive. The rejection of claims 1 and 2 has been withdrawn.

Applicant's arguments, see pages 7-8, filed 10/28/04, with respect to 102(a) by Heller have been fully considered and are persuasive. The rejection of claims 1 and 2 has been withdrawn.

Applicant's arguments, see page 8, filed 10/28/04, with respect to 102(e) by Monahan et al. have been fully considered and are persuasive. The rejection of claims 1 and 2 has been withdrawn.

Applicant's arguments, see pages 9-10, filed 10/28/04, with respect to 102(e) by Heller et al. have been fully considered and are persuasive. The rejection of claims 1, 2, and 11 has been withdrawn.

Applicant's arguments, see pages 10-11, filed 10/28/04, with respect to 102(e) by Heller et al. have been fully considered and are persuasive. The rejection of claims 1 and 2 has been withdrawn.

Applicant's arguments, see page 11, filed 10/28/04, with respect to 102(e) by Gilbert et al. have been fully considered and are persuasive. The rejection of claims 1 and 2 has been withdrawn.

Applicant's arguments, see page 11, filed 10/28/04, with respect to 102(f) by Heller et al.; Heller et al.; Gilbert et al.; and Jaroszeski et al. have been fully considered and are persuasive. The rejection of claims 1, 2, and 11 has been withdrawn.

Applicant's arguments, see page 11, filed 10/28/04, with respect to double patenting by Heller et al.; Heller et al.; Gilbert et al.; and Jaroszeski et al. have been fully considered and are persuasive. The rejection of claims 1, 2, and 11 has been withdrawn.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Whiteman whose telephone number is (571) 272-0764.

The examiner can normally be reached on Monday through Friday from 7:00 to 4:00 (Eastern Standard Time), with alternating Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang, acting SPE – Art Unit 1635, can be reached at (571) 272-0811.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Brian Whiteman
Patent Examiner, Group 1635

Joe Woitach
AU 1632